REMARKS

Claims 1-30 and 38-53 were pending in the application as of the issuance of the Office Action. Claims 8-26, 46 and 51 are withdrawn as being drawn to a non-elected invention. In the foregoing amendments, claims 1-4, 27, 28, 38, 41, 45, and 48-50 have been amended, claim 44 has been cancelled without prejudice, and new claims 54-64 have been added. Accordingly, after the amendments presented herein have been entered, claims 1-30 and 38-64 will remain pending in this application.

Support for the amended and newly added claims can be found throughout the specification and in the claims as originally filed. Specifically, support for the amended and newly added claims can be found at, for example, page 2, line 28 to page 3, line 4; page 6, line 15 to page 6, line 30; page 8, line 31 to page 9, line 5; and page 32, line 32 to page 33, line 2 of the specification. No new matter has been added. Accordingly, Applicants request that the new claims be entered.

Amendments to the claims should in no way be construed as an acquiescence to any of the Examiner' rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

I. Requirement for Election/Restriction

Applicants acknowledge the election of Group I, *i.e.,* claims 1-7, 27-30, and 38-44, in response to the Restriction Requirement under 35 U.S.C. § 121 as set forth in the Office Action of October 11, 2006. Applicants additionally acknowledge the ***species*** election of SEQ ID NO:2. With respect to the elected species of SEQ ID NO:2, it is applicants understanding that the election of a specific species is for search purposes only, and that, upon allowance of the elected claims, the generic claims also will be searched, and Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141.

With regard to the requirement to elect a single target CMV gene, Applicants respectfully request reconsideration with respect to the requirement for restriction to a

single target CMV gene selected from IE1 and IE2, in view of the foregoing amendments to the claims. In particular, the claims as amended specify methods and compositions comprising an RNAi agent, *wherein the RNAi agent targets the CMV transcript within a region common to at least two CMV mRNAs derived from the transcript*. As the mRNAs encoding IE1 and IE2 are derived from a common, alternatively spliced RNA transcript, and the claims as amended specify that the region targeted by the RNAi agents of the invention is shared among mRNAs derived from a common transcript, Applicants submit that the RNA transcript encoding the proteins IE1 and IE2 should be examined together, *i.e.*, as a single target CMV gene.

II. Objections to the Specification

The Examiner has objected to the title of the invention, and has indicated that a new title is required which is more clearly indicative of the claimed invention. Applicants have amended the title to recite "RNAi Targeting of a Cytomegalovirus (CMV)," thereby rendering this rejection moot.

III. Claim Objections

The Examiner has objected to claims 38-44 as depending from a non-elected claim, claim 51. Applicants have cancelled claim 44, and have amended claim 38, such that claim 38 (and dependent claims 39-43), now depend from elected claims 27-30, 48-50, 52, 53, 56 and 57, thereby rendering this rejection moot.

The Examiner has objected to claims 28 and 45 as containing non-elected subject matter. Applicants have amended the claims to delete reference to the non-elected inventions relating to DNA polymerase, a scaffold protease, gB and gH, thereby rendering the Examiner's rejection moot. In response to the Examiner's requirement for correction of typographical errors in claims 28 and 45, Applicants have amended the claims to replace "1E1" and "1E2" with "IE1" and "IE2", thereby rendering this rejection moot.

IV. Enablement

The Examiner has rejected claims 1-7, 38-45, and 47 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection and submit that, based on the teachings in Applicants'

specification as well as the general knowledge available in the art at the time of filing of the present application, one of skill in the art would be able to make and use the claimed invention using only routine experimentation.

Specifically, the Examiner is of the opinion that "[t]he specification, while being enabling for a method of inhibiting a CMV in a cell infected with CMV comprising administering an RNAi agent targeted to IE2 *in vitro*, does not reasonably provide enablement for a method of inhibiting a CMV in a subject infected with CMV [by] administering an RNAi agent targeted to IE2 *in vivo*, or treating retinitis in a mammal, or a pharmaceutical composition comprising the RNAi agent" (Office Action, pages 3-4). The Examiner further cites Opalinska *et al.* (Nature Reviews, 2002, 1:503-514) and Schmidt (Nature Biotechnology, 2007, 25:273-375) to demonstrate the alleged unpredictability of RNAi for *in vivo* therapeutic use, and notes that specification does not contain working examples wherein siRNAs can be used as a pharmaceutical composition to treat a condition associated with CMV infection in a vertebrate mammal.

Applicants respectfully disagree with the Examiner. Applicants assert that the claimed methods are presented with sufficient description in the specification to enable one of skill in the art to practice the invention at the time the application was filed. Applicants have made an important discovery, based on significant amounts of data, regarding a class of molecules that have utility for inhibiting CMV. This data is included in the instant application. The invention is further described throughout the specification, in which Applicants provide ample guidance regarding the structure of the molecules and how to use them. In order for a claimed invention to be enabled, the standard is not whether or not some experimentation is necessary to practice the claimed invention. Rather, the standard is whether or not the experimentation necessary to practice the claimed invention is undue (See In re Wands, 858 F.2d at 737 and MPEP 2164.02). Thus, enablement is not precluded by the necessity for some experimentation, and a considerable amount of experimentation is permitted. In re Wands, supra.

A. Cited References

As noted above, the Examiner has cited Opalinska *et al.*(2002) to support the conclusion that the claimed methods were unpredictable at the time the application was filed. Opalinska is a review article which describes sequence-specific knockdown of

mRNA using different techniques, and provides commentary on advances and challenges proposed or encountered in the field. Specifically, the Examiner refers to a passage from Opalinska stating "mRNA targeting is largely a random process, which accounts for the many experiments in which the addition of an antisense nucleic acid yields no effect on expression" (Opalinska *et al.*, page 511). Applicants respectfully assert that evaluation of the significance of this statement must be made with respect to the quoted passage as a whole. In this passage, Opalinska is specifically referring to the accessibility of mRNA in a cell (*i.e., in vivo*) to hybridization with the RNAi agent. The accessibility of particular mRNA sequences to hybridization with an RNAi agent is dictated by, for example, intramolecular base pairing and proteins that associate with mRNA in a cell. Opalinska indicates that "walks" down the mRNA sequence and computer-assisted modeling of RNA structure are potential solutions to this problem. In the instant specification, the accessibility of the targeted sequences within the RNA transcript was demonstrated experimentally, as evidenced by data indicating that cellular expression of the targeted genes is substantially reduced following transfection with SEQ ID NOs:1 and 2 (see, for example, the data presented in Figure 3 and Figure 5, described in the specification at page 41, line 30 to page 43, line 9). Applicants therefore respectfully submit that the cited passage of Opalinska is not relevant to the enablement of the claimed invention. Opalinska additionally notes that "clinical development of antisense compounds has proceeded to the point at which several nucleic-acid drugs have entered Phase I/II, and in a few cases, Phase III trials", supporting the enablement of the claimed invention. Lastly, Applicants wish to note that Opalinska was published nearly two years prior to the filing date of the instant application, and is therefore not representative of the knowledge available to a skilled artisan in this rapidly growing field at the time the invention was made.

The Examiner has also cited the post-filing reference Schmidt (2007) as evidence that the claimed invention lacks enablement. It is taught in the MPEP (section 2164.05(a)) that "In general, the examiner should not use post-filing date references to demonstrate that the patent is non-enabling. Exceptions to this rule could occur if a later-dated reference provides evidence of what one skilled in the art would have known on or before the effective filing date of the patent application." With respect to Schmidt, the Examiner has not specifically identified any teachings that are evidence of what one skilled in the art would have known on the filing date of the instant invention.

Contrary to the Examiner's assertion that the unpredictability of *in vivo* inhibitory activity and therapeutic efficacy of siRNA molecules remained unresolved in 2007, Applicants submit that a review of the post-filing art finds a plethora of research articles which support the enablement of the invention. These articles further demonstrate that siRNA may be efficiently delivered *in vivo* to many tissues (*e.g.*, brain, skin, lung, liver, intestine, eye, and tumor tissues) of a mammalian organism resulting in RNAi of the target mRNA. Applicants submit the following references in an Information Disclosure Statement for the Examiner's consideration:

1. Grzelinski, M. *et al.* RNA interference-mediated gene silencing of pleiotrophin through polyethylenimine-complexed small interfering RNAs in vivo exerts antitumoral effects in glioblastoma xenografts. Hum. Gene Ther. 17, 751–766 (2006).
2. Tan, P.H., Yang, L.C., Shih, H.C., Lan, K.C. & Cheng, J.T. Gene knockdown with intrathecal siRNA of NMDA receptor NR2B subunit reduces formalin-induced nociception in the rat. Gene Ther. 12, 59–66 (2005).
3. Thakker, D.R. *et al.* Neurochemical and behavioral consequences of widespread gene knockdown in the adult mouse brain by using nonviral RNA interference. Proc. Natl. Acad. Sci. USA 101, 17270–17275 (2004).
4. Hu-Lieskovan, S., Heidel, J.D., Bartlett, D.W., Davis, M.E. & Triche, T.J. Sequence-specific knockdown of EWS-FLI1 by targeted, nonviral delivery of small interfering RNA inhibits tumor growth in a murine model of metastatic Ewing's sarcoma. Cancer Res. 65, 8984–8992 (2005).
5. Zhang, Y. *et al.* Engineering mucosal RNA interference in vivo. Mol. Ther. 14, 336–342 (2006).
6. Li, B. *et al.* Using siRNA in prophylactic and therapeutic regimens against SARS coronavirus in Rhesus macaque. Nat. Med. 11, 944–951 (2005).
7. Soutschek, J. *et al.* Therapeutic silencing of an endogenous gene by systemic administration of modified siRNAs. Nature 432, 173–178
8. Zimmermann, T.S. *et al.* RNAi-mediated gene silencing in non-human primates. Nature 441, 111–114 (2006).
9. Reich, S.J. *et al.*, Small interfering RNA (siRNA) targeting VEGF effectively inhibits ocular neovascularization in a mouse model. *Mol. Vis.* 9, 210–216 (2003)

Grzelinski *et al.* discuss the systemic delivery of siRNA to nude mice via subcutaneous and intraperitoneal injection using the well-known nucleic acid transfection reagent polyethyleneimine (PEI). Delivery of siRNA directed against the pelitrophin (PTN) growth factor resulted in efficient knockdown of target mRNA in subcutaneous tumor xenografts, as well as significant inhibition of tumor growth. Moreover, intracranial injection of siRNAs into the CNS resulted in efficient knockdown of the PTN target mRNA and anti-tumor effects in an orthotopic mouse model of glioblastoma.

Tan *et al.* further investigated the use of PEI-mediated siRNA delivery to the CNS via intrathecal injection *in vivo*. siRNAs directed against N-methyl-D-aspartate (NMDA) receptors were reported to knockdown NMDA receptor protein levels in the spinal cord of a rat model and reduce nociception *in vivo*.

Thakker *et al.* investigated the delivery of siRNA into brain cells via infusion of siRNA into the ventricular system of the brain. siRNAs directed against the dopamine transporter (DAT) were reported to achieve global downregulation of DAT protein levels in the brain and elicit a behavioral response that is similar to that obtained with a pharmacologically selective DAT inhibitor.

Hu-Lieskovan *et al.* investigated the *in vivo* systemic delivery of siRNA in a mouse model of Ewing's sarcoma, a metastatic cancer, *in vivo*. siRNA directed against the Ewing's Sarcoma gene *EWS-FLI1* were reported to achieve knockdown of the *EWS-FLI1* gene and inhibition of tumor growth was observed.

Zhang *et al.* investigated the delivery of siRNA into the intestine of a mouse model of inflammatory bowel disease *in vivo* by vaginal or rectal administration. siRNA directed against TNFalpha was reported to achieve knockdown of the target mRNA in mucosal tissues, resulting in mucosal resistance to experimental colitis.

Li *et al.* investigated the administration of siRNA into non-human primate lungs *in vivo* via direct intranasal administration. siRNA directed against target mRNAs encoded by Severe Acute Respiratory syndrome (SARS) coronavirus (SCV) were reported to result in a reduction of both SCV viral levels and SARS symptoms.

Soutschek *et al.* investigated the administration of siRNA to the liver and jejunum of mice *in vivo* via tail vein injection. Cholesterol-conjugated siRNAs directed against apoB target mRNA resulted in knockdown of the apoB mRNA in liver and jejunum and a concomitant reduction in the physiological levels of total cholesterol.

Zimmermann *et al.* discuss the administration of siRNA to the liver in non-human primates *in vivo* via intravenous injection. Liposome encapsulated siRNAs directed against apoB target mRNA lead to dose-dependent silencing of apoB mRNA expression in the liver and resulted in significant reductions in ApoB protein, serum cholesterol and low-density lipoprotein levels that lasted for 11 days.

In summary, some of the teachings of the references cited by the Examiner are directed to RNAi technology, but they do not establish the unpredictability of the claimed

invention at the time the patent application was filed. Moreover, the post-filing art is replete with teachings which support the enablement of the invention. It is correct that some commentators have identified areas where improvements in the technology are needed. Like any nascent technology, RNAi presents many opportunities for improvements and development, and although many improvements and alternative delivery strategies have been developed since the invention was made by Applicants, the invention can be practiced as claimed and described in the instant application using techniques available in the art at the time of filing using no more than routine experimentation.

B. Retinitis

With respect to claims directed specifically to the treatment of retinitis, Applicants note that Opalinska *et al.* (2002) describes the FDA approval of the antiviral drug Vitravene (sodium fomivirsen) in 1998. Vitravene is a single-stranded 21-mer phosphorothioate DNA oligonucleotide which has a sequence complementary to mRNA transcribed from CMV. Vitravene is administered by intravitreal injection for the treatment of CMV-induced retinitis. Given the clinical efficacy of Vitravene for gene silencing in the eye, it is highly predictable that the RNAi agents of the invention would be at least as effective for gene silencing in the eye if delivered in a similar manner. Indeed, administration of siRNA to the eye (*e.g.,* via intravitreal injection) has been shown to be effective for silencing of disease-associated target mRNAs such as Vascular Endothelial Growth Factor (VEGF) in the eye (see, *e.g.*, Reich, S.J. *et al.*, Small interfering RNA (siRNA) targeting VEGF effectively inhibits ocular neovascularization in a mouse model. *Mol. Vis.* 9, 210–216 (2003)). With respect to the Examiner's assertion that "reduced IE2 expression levels are not indicative of treating a CMV-associated disease (*e.g.,* retinitis, prostate cancer), Applicants submit that, in addition to the teachings provided in the specification, it was well-known in the art at the time of filing that compounds which inhibit IE2 (*e.g.,* Vitravene) had successfully been used to treat retinitis associated with CMV infection.

The Examiner additionally states that "with regard to the instantly claimed method wherein the retinitis is treated via intravitreal injection of siRNA, Schmidt teaches that siRNAs must reach internal organs through systemic delivery routes and this delivery problem still remains at large" (Office Action, page 6). Applicants respectfully submit that this is a mischaracterization of the teachings of Schmidt with respect to intravitreal

injection. Schmidt in fact teaches that some companies have *avoided* targets requiring systemic delivery of siRNA, and have instead pursued targets whereby the RNAi agents can be delivered locally (see Schmidt, page 275, third column). As an example, Schmidt cites Acuity's siRNA product bevasiranib, which is injected directed into the eye, and has performed well in Phase II clinical trials. In view of the foregoing, Applicants respectfully submit that one skilled in the art would be able to practice the instantly claimed methods directed to the treatment of retinitis using the teaching provided in the specification and techniques known in the art at the time of filing of the instant application using no more than routine experimentation.

C. In vivo *Working Examples*

To further support the rejection of the pending claims as allegedly failing to comply with the enablement requirement, the Examiner alleges that the instant specification does not provide working examples wherein siRNAs can be used as a pharmaceutical composition to treat a condition associated with CMV infection in a mammal. Applicants respectfully direct the Examiner's attention to M.P.E.P. § 2164.02, which provides that the absence of a working example is not sufficient to undermine the enablement of a claimed invention. Indeed, as provided by this section:

> An *in vitro* **or** *in vivo* animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention...[I]f the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. Even with such evidence, the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. *In re Brana,* 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995)(reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications). Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an in vitro or an in vivo animal model. **A rigorous or an invariable exact correlation is not required** (emphasis added).

Applicants note that the specification does provide working examples wherein administration of the RNAi agents of the invention to human fibroblasts infected with human cytomegalovirus (HCMV) results in substantial knockdown of IE1 and IE2 gene expression. This RNAi-mediated suppression of HCMV gene expression inhibited virus

replication in these human cells, as evidenced by a five-fold reduction in virus titer following administration of siRNA (see, for example, Examples 1 and 2 at page 41, line 30 to page 44, line 9 of the specification, and Figures 3 and 5-7). The strict species-specificity of HCMV for human and primate cells precludes preclinical evaluation of potential therapeutic agents in animal models. Inhibition of HCMV in human cells is a pre-clinical model system that is widely accepted in the art, and a close correlation has been observed between inhibition of HCMV infection in human cells and treatment of HCMV infection in *in vivo* clinical trials using human subjects. In support of this assertion, Applicants submit the following reference in an Information Disclosure Statement: Smet et al., "Fomivirsen-a phosphorothioate oligonucleotide for the treatment of CMV retinitis," *Ocular Immunology and Inflammation* 7(3-4): 189-198 (1999). As described in this reference, the antisense oligonucleotide Fomivirsen successfully inhibited CMV replication in human fibroblast cells and human retinal pigment epithelial cells, and was then successfully tested in clinical trials in human subjects, wherein intravitreal injection of the compound to patients with CMV treated CMV-associated retinitis (see, for example, page 192-194). This compound was not evaluated with respect to efficacy in inhibiting HCMV in *in vivo* animal models, for the reasons noted above.

With respect to pharmaceutical compositions comprising an RNAi agent, Applicants respectfully submit that the specification provides ample guidance regarding the composition and preparation of pharmaceutical formulations suitable for administration of the RNAi agents of the invention through a wide range of administration routes commonly used in the art. These pharmaceutical compositions are described in the specification at, for example, page 2, line 28 to page 3, line 4, and at page 32, line 23 to page 37, line 27. In addition to the pharmaceutical compositions provided in the specification, one of skill in the art would also recognize that pharmaceutical compositions comprising a nucleic acid molecule known in the art and used for therapeutic treatment of, *e.g.,* retinitis, would additionally be suitable for practicing the methods of the invention.

In view of the foregoing evidence, Applicants respectfully submit that the teachings of the present specification, alone or in combination with the knowledge available in the art at the time of filing of the present application, are sufficient to allow a skilled artisan to practice the claimed invention. One of skill in the art would be able to make and use the

RNAi agents of the invention to inhibit CMV, and to treat a condition associated with CMV infection, using only routine experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

IV. Written Description

The Examiner has rejected claims 1-7, 27-30, 38-45, 48-50, and 53 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Specifically, the Examiner notes that the specification must provide sufficient distinguishing identifying characteristics of the genus of claimed anti-CMV RNAi agents by disclosing their structure/function correlation. The Examiner asserts that the two siRNA molecules of SEQ ID NO:1 and SEQ ID NO:2, described in the working examples of the specification, do not constitute a representative number of species embraced by the claimed genus.

Applicants respectfully traverse the Examiner's rejection. Applicants respectfully submit that the two siRNA molecules of SEQ ID NOs: 1 and 2 are sufficiently representative of the genus of anti-CMV RNAi agents as claimed. The specification provides guidance with respect to the regions of the CMV genome which are suitable targets for RNAi (see, for example, page 7, line 14 to page 9, line 5 of the specification). The nucleotide sequence of these regions was known in the art at the time of filing of the instant application, and is additionally described in the specification (see, for example, page 9, line 6 to page 9, line 24 and SEQ ID NOs:177-183). The specification further describes how to use design siRNA molecules targeting these sequences (see, for example, page 9, line 25 to page 10, line 1), and provides 169 examples of specific siRNA sequences which target CMV genes (see SEQ ID NOs:7-176). Methods of designing siRNAs targeting a given gene sequence were additionally well known in the art at the time of filing. As evidence supporting this assertion, applicants submit in the accompanying Information Disclosure Statement the article "Designing a Better siRNA" (Ambion TechNotes 10(4), September 2003). This reference describes an algorithm useful for designing highly effective siRNA sequences. As evidenced by this article, procedures for designing and producing siRNAs based on the nucleotide sequence of gene were readily available to those of skill in the art, and consequently the design and production of siRNAs targeting a known

nucleotide sequence was conventional and routine at the time of filing of the instant application. When considering the distinguishing characteristics of the claimed invention, the CMV nucleic acid sequences provided in the specification and known in the art defines and limits the structure of any effective RNAi agent. The RNAi molecules are also defined functionally, *i.e.,* by their ability to inhibit CMV. Methods of screening RNAi agents (*e.g.,* siRNA molecules) to test for this functional activity were known in the art and are additionally described in the working examples of the specification, in which two members of the claimed genus are reduced to practice. For each of the foregoing reasons, Applicants submit that the genus of claimed RNAi molecules which inhibit a CMV are sufficiently described in the specification to demonstrate to a skilled artisan that Applicants were in possession of the claimed invention at the time of filing. Applicants, therefore, respectfully request reconsideration and withdrawal of the rejection of claims 1-7, 27-30, 38-45, 48-50, and 53 under 35 U.S.C. § 112, first paragraph, as lacking written description.

V. 35 U.S.C. § 103(a)

The Examiner alleges that the above-identified claims are rendered obvious by the teachings of Kondo et al. (U.S. Patent No. 5,783,383) in view of Fire et al. (U.S. Patent No. 6,506,559) and Tuschl et al. (U.S. Patent No. 7,056,704). In particular, the Examiner alleges that Kondo teaches the DNA sequence of the IE2 transcript, in addition to a method of detecting CMV infection in a cell by PCR amplification, and expression vectors for expressing antisense RNA or ribozymes for gene inhibition applications. The Examiner also notes that the PCR primer of SEQ ID NO:19 of Kondo is complementary to nucleotides of 1-18 of the instantly claimed SEQ ID NO:2. The Examiner acknowledges that Kondo does not teach a method of inhibiting CMV expression comprising an RNAi agent, and relies on Fire and Tuschl with respect to their teachings regarding RNAi and siRNA-mediated gene inhibition. The Examiner specifically alleges that "[i]t would have been obvious...to use the RNAi-mediated inhibition of Fire et al. to target the IE2 transcript of CMV of Kondo et al. by designing an siRNA molecule as taught by Tuschl et al.", and one of ordinary skill in the art would have had a reasonable expectation of success in doing so because "the CMV gene, especially the IE2 gene, was a well-known target for antisense-mediated gene therapy as taught by Kondo et al."

Applicants respectfully traverse this rejection. As an initial matter, Applicants note

that the claims, as amended, specify that the RNAi agents used in the methods of the invention target the CMV transcript within a region common to at least two CMV mRNAs derived from the transcript. Kondo does not teach or suggest this important feature of the invention, and Fire and Tuschl fail to remedy this deficiency. In contrast to the Examiner's assertion, Applicants additionally submit that Kondo does not, in fact, teach targeting of the CMV IE2 gene using antisense molecules and ribozymes, but rather teaches that the promoter sequence which drives expression of CMV genes IE1/IE2 can be incorporated into an expression vector, from which the promoter would drive expression of heterologous nucleic acid sequences in a cell containing such a vector during CMV infection. Kondo notes that such heterologous nucleic acid sequences may encode, e.g., antisense RNA or ribozymes, but does not provide speculation regarding potential antisense or ribozyme targets. Kondo therefore does not teach inhibition of CMV by using antisense or ribozymes to target IE2. Applicants further wish to point out that the nucleic acid molecule of SEQ ID NO:19 of Kondo is a single-stranded, 20-nucleotide DNA molecule used as a primer for PCR amplification. Kondo does not teach or suggest that this molecule, or a molecule complementary to part of this nucleic acid sequence (i.e., SEQ ID NO:2 of the instant application), can be used to target the CMV IE1/IE2 gene through RNA interference. Accordingly, Applicants submit that Kondo, alone or in combination with Fire and Tuschl, fails to teach or suggest methods or compositions comprising an RNAi agent that targets the CMV transcript within a region common to at least two CMV mRNAs derived from the transcript, as required by the amended claims. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. § 103(a).

If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Dated: **November 30, 2007**

Respectfully submitted,

By_____

Debra J. Milasincic, Esq.
Registration No.: 46,931
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109-2127
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant